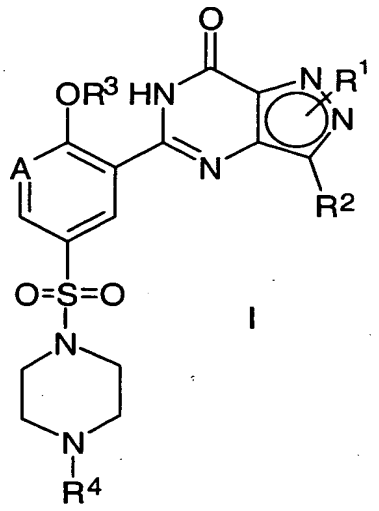
Claims

1. A process for the production of a compound of general formula I:



I

wherein

A represents CH or N;

R^1 represents H, lower alkyl (which alkyl group is optionally interrupted by O), Het, alkylHet, aryl or alkylaryl, which latter five groups are all optionally substituted (and/or, in the case of lower alkyl, optionally terminated) by one or more substituents selected from halo, cyano, nitro, lower alkyl, OR^5, $C(O)R^6$, $C(O)OR^7$, $C(O)NR^8R^9$, $NR^{10a}R^{10b}$ and $SO_2NR^{11a}R^{11b}$;

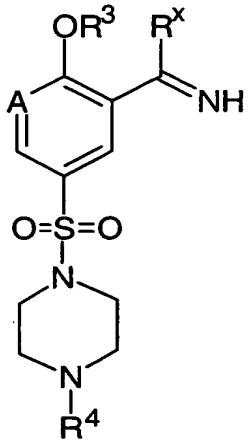
R^2 and R^4 independently represent lower alkyl;

R^3 represents lower alkyl, which alkyl group is optionally interrupted by oxygen;

Het represents an optionally substituted four- to twelve-membered heterocyclic group, which group contains one or more heteroatoms selected from nitrogen, oxygen and sulfur;

R^5, R^6, R^7, R^8, R^9, R^{11a} and R^{11b} independently represent H or lower alkyl; R^{10a} and R^{10b} either independently represent, H or lower alkyl or, together with the nitrogen atom to which they are attached, represent azetidinyl, pyrollidinyl or piperidinyl,

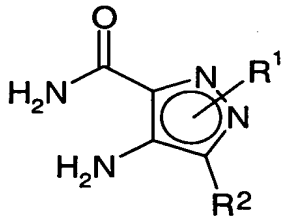
which process comprises the reaction of a compound of formula II,



II

wherein R^x is a group substitutable by an aminopyrazole and A, R^3 and R^4 are as defined above,

with a compound of general formula III,



III

wherein R^1 and R^2 are as defined above.

2. A process as claimed in Claim 1, wherein, in the compound of general formula I, R^1 represents C_{1-4} alkyl, which alkyl group is optionally interrupted by an oxygen atom, and/or is optionally terminated by a Het group.

3. A process as claimed in Claim 2, wherein R^1 represents linear C_{1-3} alkyl, which alkyl group is optionally interrupted by an oxygen atom, or is optionally terminated by a 2-pyridinyl group.

4. A process as claimed in any one of the preceding claims, wherein, in the compound of general formula I, R^2 represents C_{1-4} alkyl.

5. A process as claimed in Claim 4, wherein R^2 represents linear C_{2-3} alkyl.

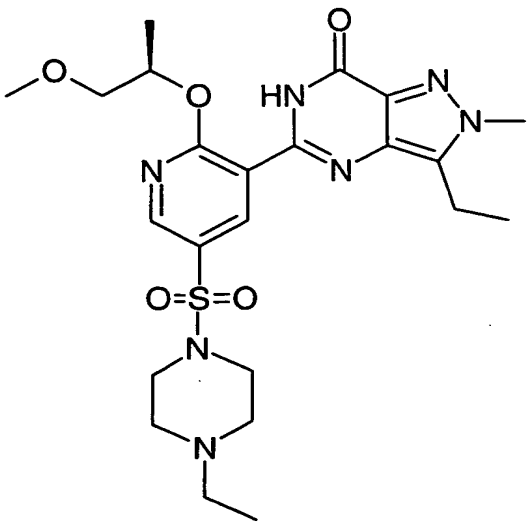
6. A process as claimed in any one of the preceding claims, wherein, in the compound of general formula I, R^3 represents C_{1-5} alkyl, which alkyl group is optionally interrupted by an oxygen atom.

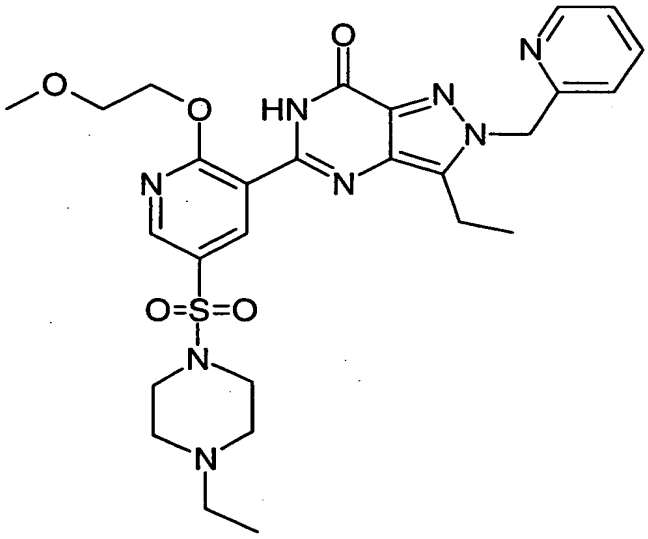
7. A process as claimed in Claim 6, wherein R^3 represents linear or branched C_{2-4} alkyl, which alkyl group is optionally interrupted by an oxygen atom.

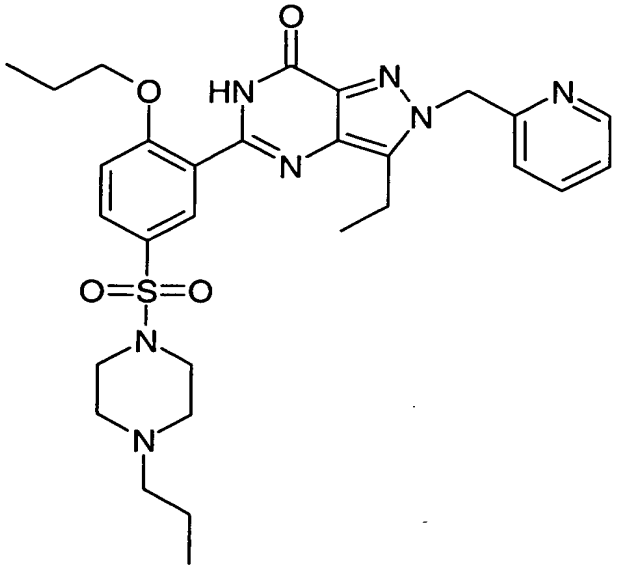
8. A process as claimed in any one of the preceding claims, wherein, in the compound of general formula I, R^4 represents C_{1-3} alkyl.

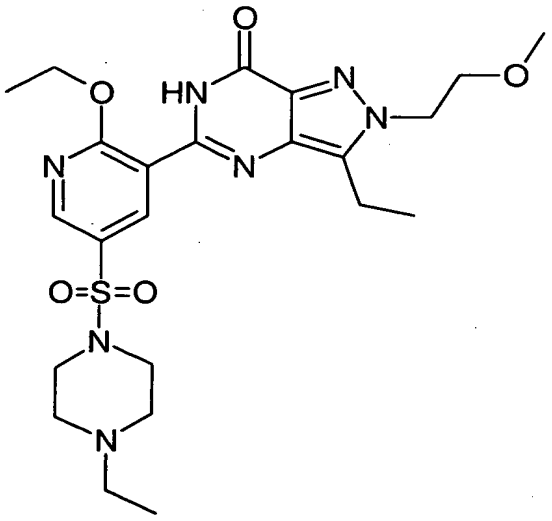
9. A process as claimed in Claim 8, wherein R^4 represents C_{1-2} alkyl.

10. A process as claimed in any one of the preceding claims, wherein the compound is selected from sildenafil, or any one of the following four compounds









11. A process as claimed in any one of the preceding claims, wherein the group R^x of the compound of formula II represents $-NH_2$, $-NHR^a$, $-N(R^b)R^c$, $-SR^d$, -SH, $-OR^e$ (in which groups R^a to R^e each independently represent the same groups that R^1 as defined in Claim 1 may represent, except that they do not represent H) or halo.

12. A process as claimed in Claim 11, wherein R^x represents $-NHR^a$, $-N(R^b)R^c$, $-SR^d$, -SH or $-OR^e$.

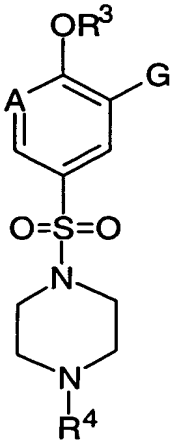
13. A process as claimed in Claim 12, wherein R^x represents ethoxy.

14. A process as claimed in any one of the preceding claims, wherein the reaction is carried out in the presence of a solvent system that includes an aromatic hydrocarbon, chlorobenzene or a solvent of formula R^xH, wherein R^x is as defined in any one of Claims 1 or 11 to 13.

15. A process as claimed in Claim 14, wherein the solvent is toluene, xylene, chlorobenzene or ethanol.

16. A process as claimed in Claim 14 or Claim 15, wherein the reaction is carried out at reflux temperature.

17. A process as claimed in any one of the preceding claims, wherein the compound of formula II is prepared by way of reaction of a compound of formula IV,



IV

wherein G represents a carboxylic acid group (-C(O)OH) or a derivative thereof, and A, R^3 and R^4 are as defined in any one of Claims 1 and 6 to 10

(as appropriate), with an appropriate reagent for converting the group G to a $-C(R^x)=NH$ group, wherein R^x is as defined in any one of Claims 1 or 11 to 13.

18. A process as claimed in Claim 17, wherein, in the compound of formula IV, the group G represents -CN, $-C(OR^e)_3$, $-C(O)NH_2$ or $-C(=NOR^f)NR_2$, wherein R^f represents H or lower alkyl and R^e is as defined in Claim 11.

19. A process as claimed in Claim 18, wherein, when R^x represents $-OR^e$ (wherein R^e represents lower alkyl (optionally interrupted by O), alkylHet or alkylaryl):

(a) a corresponding compound of formula IV in which G represents -CN is reacted with an alcohol of formula VA,

$$R\alpha OH \qquad VA$$

wherein $R\alpha$ represents lower alkyl (optionally interrupted by O), alkylHet or alkylaryl, and Het is as defined in Claim 1, in the presence of a protic acid;

(b) a corresponding compound of formula IV in which G represents $-C(O)NH_2$ is reacted with an appropriate alkylating agent of formula VB,

$$R\alpha\text{-}Z^1 \qquad VB$$

wherein Z^1 represents a leaving group and $R\alpha$ is as defined above; or

(c) a corresponding compound of formula IV in which G represents $-C(OR\alpha)_3$, wherein $R\alpha$ is as defined above, is reacted with ammonia, or an *N*-protected derivative thereof.

20. A process as claimed in Claim 18, wherein, when R^x represents $-OR^e$ (wherein R^e represents Het or aryl), a corresponding compound of formula IV in which G represents -CN is reacted with a compound of formula VC,

$$R_\beta OH \qquad VC$$

wherein R_β represents Het or aryl, and Het is as defined in Claim 1.

21. A process as claimed in Claim 18, wherein, when R^x represents $-NH_2$:

(a) a corresponding compound of formula IV in which G represents -CN is reacted with hydrazine, hydroxylamine or *O*-lower alkyl hydroxylamine, followed by reduction of the resultant intermediate under standard conditions; or

(b) a corresponding compound of formula IV in which G represents $-C(=NOR^f)NR_2$, wherein R^f is as defined in Claim 18, is reduced under standard conditions.

22. A process as claimed in Claim 18, wherein, when R^x represents $-NH_2$, $-NHR^a$ or $-N(R^b)R^c$, a corresponding compound of formula IV in which G represents -CN is reacted with a compound of formula VD,

$$HN(R_\chi)(R_\delta) \qquad VD$$

wherein R_χ and R_δ independently represent H or R^a, and R^a is as defined in Claim 11.

23. A process as claimed in Claim 18, wherein, when R^x represents -SH:

(a) a corresponding compound of formula IV in which G represents -CN is reacted with hydrogen sulfide; or

(b) a corresponding compound of formula IV in which G represents $-C(O)NH_2$ is reacted with a reagent that effects oxygen-sulfur exchange.

24. A process as claimed in Claim 18, wherein, when R^x represents $-SR^d$, a corresponding compound of formula IV in which G represents -CN is reacted with a compound of formula VE,

$$R^dSH \qquad \text{VE}$$

wherein R^d is as defined in Claim 11.

25. A process as claimed in Claim 18, wherein, when R^x represents halo, a corresponding compound of formula IV in which G represents $-C(O)NH_2$ is reacted with a halogenating agent.

26. A process as claimed in any one of Claims 1 to 16, wherein the compound of formula II is prepared by way of reaction of another compound of formula II with a reagent that will convert one R^x group to another, wherein R^x is as defined in any one of Claims 1 or 11 to 13.

27. A process as claimed in Claim 26, wherein, when R^x represents $-OR^e$ (wherein R^e represents lower alkyl, alkylHet or alkylaryl), a corresponding compound of formula II in which R^x represents Cl is reacted with a compound of formula VA, as defined in Claim 19.

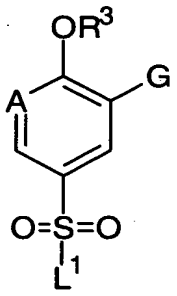
28. A process as claimed in Claim 26, wherein, when R^x represents $-NH_2$, $-NHR^a$ or $-N(R^b)R^c$, a corresponding compound of formula II in which R^x represents Cl, -SH, $-SR^d$ or $-OR^e$, wherein R^d and R^e are as defined in Claim 11, is reacted with an appropriate compound of formula VD, as defined in Claim 22, or an acid addition salt thereof.

29. A process as claimed in Claim 26, wherein, when R^x represents $-SR^d$, a corresponding compound of formula IV in which R^x represents -SH is reacted with a compound of formula VF,

$$R^d\text{-}Z^2 \qquad \text{VF}$$

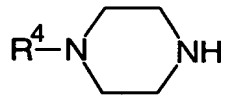
wherein Z^2 represents a leaving group and R^d is as defined in Claim 11.

30. A process as claimed in any one of Claims 17 to 25, wherein the compound of formula IV is prepared by reaction of a compound of formula VI,



VI

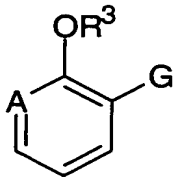
wherein L^1 is a leaving group and A, G and R^3 are as defined in any one of Claims 1, 6, 7, 10, 17 and 18 (as appropriate), with a compound of formula VII,



VII

wherein R^4 is as defined in any one of Claims 1 and 8 to 10.

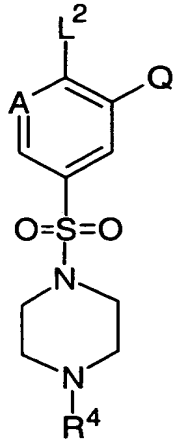
31. A process as claimed in Claim 30, wherein the compound of formula VI is prepared by reaction of a compound of formula VIII,



VIII

wherein A, G and R^3 are as defined in any one of Claims 1, 6, 7, 10, 17 and 18 (as appropriate), with a reagent that may be used for the introduction of a $-SO_2L^1$ group into an aromatic or heteroaromatic ring system.

32. A process as claimed in any one of Claims 17 to 24, wherein the compound of formula IV is one in which G represents -CN or $-C(O)NH_2$, and is prepared by reaction of a compound of formula IX,



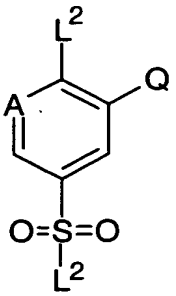
IX

wherein Q represents -CN or $-C(O)NH_2$, L^2 represents a leaving group and A and R^4 are as defined in any one of Claims 1 and 8 to 10, with a compound that will provide the group R^3O.

33. A process as claimed in Claim 32, wherein the compound that will provide the group R^3O is a lower alkyl alcohol.

34. A process as claimed in Claim 32 or 33, wherein the leaving group L^2 is chloro.

35. A process as claimed in any one of Claims 32 to 34, wherein the compound of formula IX is prepared by reaction of a compound of formula X,



X

wherein Q and L^2 are as defined in Claim 32, and A is as defined in Claim 1, with a compound of formula VII as defined in Claim 30.

36. A process as claimed in any one of Claims 17 to 24, wherein the compound of formula IV is one in which G represents -CN, and is prepared by dehydration of a corresponding compound of formula IV in which G represents $-C(O)NH_2$.

37. A process as claimed in any one of Claims 17 to 19, 23 and 25, wherein the compound of formula IV in which G represents $-C(O)NH_2$ is prepared from a corresponding compound of formula IV in which G represents -C(O)OH by reaction with ammonia or a derivative thereof.

38. A compound of formula II, as defined in any one of Claims 1 and 11 to 13.

39. A compound according to Claim 38 wherein A represents –CH, R^3 represents Et, R^4 represents Me and R^x represents NH_2.

40. A compound according to Claim 38 wherein A represents –CH, R^3 represents Et, R^4 represents Et and R^x represents NH_2.

41. A compound of formula IV, as defined in Claim 17 or Claim 18.

42. A compound according to Claim 39 wherein A represents N, R^3 represents Et, R^4 represents Et and G represents CO_2H.

43. A compound according to Claim 39 wherein A represents N, R^3 represents Et, R^4 represents Et and G represents CO_2Et.

44. A compound according to Claim 39 wherein A represents -CH, R^3 represents Et, R^4 represents Et and G represents CN.

45. A compound according to Claim 39 wherein A represents -CH, R^3 represents Et, R^4 represents Me and G represents CN.